

ALTERATIONS OF ONCOGENES EXPRESSION IN HUMAN NK CELLS IN CANCER PATIENTS

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Introduction. C-kit/SCF signaling play a key role in regulating NK cell homeostasis, maturation, proliferation and cytotoxicity. C-kit-deficiency in NK results in significant reduction of their, suggesting imperative role fore-kit signaling in NKcell immunobiology. We have recently showed that human NK cells express not only c-kit-receptor, but also both membrane-bound and soluble forms of c-kit ligand - Stem cell factor. The goal of this study was to characterize the c-kit/SCF autocrine loop in peripheral blood NK cells obtained from patients with cancer.

Methods. Peripheral blood specimens were collected from 17 patients (median age 62, (53-79) with different types of cancer.

Purification of NK cells and separation on c-kit positive and c-kit negative NK subsets.

PBMC were isolated from the peripheral blood by Ficoll-Paque™ PLUS (Life Technologies, USA) density gradient centrifugation (centrifuge 2-16k; Sigma, Germany). NK cells were negatively selected using DynaMag™-5 Magnet with Dynabeads® Untouched™ Human NK Cells isolation kit (Life Technologies, USA). After negative selection of NK cells, c-kit- positive and c-kit-negative subsets of NK cells were separated using human CD117 (anti-c-kit antibody) covered microbeads (Miltenyi Biotec, Germany). Using qRT-PCR, we have characterized expression of c-kit and two forms of SCF in patients' NK cells and correlated these results with the expression of c-myc. Mann-Whitney Rank Sum test was used to evaluate the statistical significance of differences between cancer patients and healthy donors. All results are expressed as the mean ± SEM. A p value, 0.05 was considered significant.

Results. We determined c-myc, c-kit, membrane-bound SCF (mbSCF) and soluble SCF (sSCF) expression in NK cells in patients with different types of cancer. Our results revealed a strong correlation between the c-myc and c-kit gene expression in NK cells in both healthy donors and cancer patients. Importantly, in patients with cancer, the level of the oncogene expression was associated with the stage and severity of the disease.

Conclusion. We suggest that abnormal signaling and expression of c-kit/SCF and c-myc is responsible for abnormal cytotoxic activity of NK cells in cancer.